REMARKS

Claims 1, 18-22, and 35 have been amended. Claims 1, 18-23, 30, and 35 are pending in the instant application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

Applicants wish to thank Examiner Mertz for her participation in a telephonic Interview with Applicants' representatives Pat Gattari and Donald Zuhn on July 15, 2008 to discuss proposed amendments to the claims for addressing possible issues under 35 U.S.C. § 112, first and second paragraphs. Agreement with respect to the claims was not reached during the Interview. In response to the Interview, Applicants submitted an Amendment on July 16, 2008.

1. Rejection of claims 1, 18-23, 30, and 35 under 35 U.S.C. § 112, first paragraph

a. Rejection of claims 1, 18-23, 30, and 35 under the written description requirement of 35 U.S.C. § 112, first paragraph

The Office Action maintains the rejection of claims 1, 18-23, 30, and 35 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that the rejection is maintained for reasons of record set forth at pages 2-6 of the Office action mailed August 22, 2008. The Action asserts that:

> [E]xcept for a trimeric polypeptide comprising three monomers, wherein each monomer comprises the amino acid sequence set forth in SEQ ID NO:106 or SEQ ID NO:107[] or SEQ ID NO:108, and each monomer comprises a specific cytokine binding domain and a tetranectin trimerising domain wherein the tetranectin trimerising domain comprises the amino acid sequence of SEQ ID NO:81, Applicants have failed to provide a written description for any other trimeric polypeptide.

In support of the above assertion, the Action cites *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004); and *Noelle v. Lederman*, 355 F.3d 1343 (Fed. Cir. 2004). In particular, the Action asserts that *University of Rochester* – in which "the inventors could not be said to have 'possessed' the claimed invention without knowing of a compound or method certain to

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produce the compound," and the asserted patent thus "constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compounds defined only by their desired properties" – is similar to the situation here. The Action concludes that in view of *University of Rochester*, the full breadth of the claims fails to meet the written description requirement. With respect to *Noelle*, the Action states that "the Court in *Noelle* concluded that as long as an applicant has disclosed a 'fully characterized antigen,' either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." The Action then asserts that "the CAFC decisions in *Noelle* and *University of Rochester* are controlling precedents for the claims in the instant case and it is suggested that Applicant visit these decisions."

In response to Applicants' assertion that the of the 36 amino acid residues that form the tetranectin trimerising structural element (TTSE), fifteen are conserved in human and murine tetranectin, the Action states that "contrary to Applicants arguments, there are more amino acids between human TTSE and murine TTSE that are not conserved compared to those that are conserved." As a result, the Action concludes that "other than the tetranectin trimerising domain set forth in SEQ ID NO:81, Applicants have failed to provide an adequate written description of the trimeric polypeptides of claims 1, 18-19." The Action further states that other than the amino acid sequences of SEQ ID NOs: 106, 107, and 108, the specification does not identify other monomers in the claimed genus of trimeric polypeptides, and therefore concludes that the distinguishing characteristics of the claimed genus of trimeric polypeptides have not been adequately described.

Applicants respectfully disagree with the Action's assertion that the specification does not provide an adequate written description of the claimed trimeric polypeptides, and contend instead that the instant application conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the claimed invention. As stated in Applicants' previous response, an inventor can show possession by describing an actual reduction to practice of the claimed invention, by a clear depiction of the invention in detailed drawings or in structural chemical formulas, or by any description of sufficient, relevant, identifying characteristics (*i.e.*, structure or other physical and/or chemical properties, functional characteristics coupled with a

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known or disclosed correlation between function and structure, or a combination of such identifying characteristics). M.P.E.P. § 2163.

Applicants note that claim 1 recites a trimeric polypeptide comprising three monomers, wherein a first portion of each monomer specifically binds a trimeric cytokine and a second portion of each monomer is a tetranectin trimerising structural element. With respect to the portion of each monomer that is a tetranectin trimerising structural element (TTSE), the specification states that TTSEs, which are responsible for trimerisation of the claimed trimeric polypeptides (specification, page 13), are described in detail in International Publication No. WO 98/56906 (the '906 publication; *i.e.*, the PCT equivalent of U.S. Application No. 11/452,434, which is discussed below in section 3). The '906 publication teaches that the human tetranectin TTSE is 36 amino acids in length (*see* Exhibit A, which shows the amino acid sequence of the full-length, mature human tetranectin monomer, and in which the human tetranectin TTSE sequence is underlined). The amino acid residues that constitute the TTSE consensus sequence are indicated by bold uppercase letters. Finally, the amino acid residues of the TTSE sequence that constitute a portion of the repeated heptad are indicated by the lowercase letters a, b, c, d, e, f, or g. Of the 36 amino acid residues that form the TTSE, fifteen are conserved in human and murine tetranectin, the C-type lectin of bovine cartilage, and the C-type lectin of shark cartilage. The conserved residues are found at positions 26, 33, 36, 37, 40-42, and 44-51 of the full-length, mature human tetranectin sequence.

While the '906 publication teaches that the residues at positions 26, 33, 36, 37, 40-42, and 44-51 constitute the TTSE consensus sequence, the '906 publication also teaches that a number of these residues can be substituted with other amino acid residues. For example, the '906 publication teaches that the cysteine residue at position 50 "should be mutagenized to serine, threonine, methionine or to any other amino acid residue in order to avoid formation of an unwanted inter-chain disulphide bridge, uncontrolled multimerisation, aggregation and precipitation of a polypeptide product harbouring this sequence" ('906 publication, page 16, lines 9-16; the instant specification provides a similar disclosure at page 13). The '906 publication also teaches that "one advantageous embodiment of the monomer polypeptide construct of the invention is one where at least one amino acid residue selected from the group consisting of amino acid residue nos. 6, 21, 22, 24, 25, 27, 28, 31, 32, 35, 39, 41, 42, is/are substituted by any non-helix breaking amino acid residue," and further discloses that "[a]ll these residues have been shown ***not*** to be directly involved in the intermolecular

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interactions which stabilize[] the trimeric complex between three TTSEs of native tetranectin monomers and it is therefore expected that these amino acids may be safely substituted with any amino acid which will not have an adverse effect on helix formation" ('906 publication, page 21, lines 21-33; emphasis added). In addition, the '906 publication teaches that it is "preferred that the TTSE comprises a repeated heptad having the formula a-b-c-d-e-f-g (N to C), wherein residues a and d [*i.e.*, positions 26, 33, 37, 40, 44, 47, and 51] generally are hydrophobic amino acids" ('906 publication, page 22, lines 7-10). Furthermore, while the '906 publication teaches that the "a" and "d" residues of the third heptad repeat (*i.e.*, the residues at positions 44 and 47 of the amino acid sequence shown in Exhibit A) in human and murine tetranectin, the C-type lectin of bovine cartilage, and the C-type lectin of shark cartilage are glutamine, the residues at these positions are only the "most preferred" residues ('906 publication, page 22, lines 10-15).

Applicants note that a TTSE sequence that shares 68% identity with the consensus sequence shown in Figure 2 of the '906 publication would retain eleven of the fifteen residues of the consensus sequence. Similarly, a TTSE sequence that shares 75% identity would retain twelve residues, a TTSE sequence that shares 81% identity would retain thirteen residues, and a TTSE sequence that shares 87% or 92% identity would retain fourteen residues of the consensus sequence. In view of the express teachings in the '906 publication, which was published on December 17, 1998 (almost five years earlier than the filing date of the instant application), Applicants contend that one of ordinary skill in the art would readily recognize the residues of a tetranectin trimerising structural element that are tolerable to change without destroying the function of that element (*i.e.*, the ability to trimerize the monomers of the claimed trimeric polypeptides). Applicants contend that because the written description requirement can be satisfied without describing information in the specification that is well known in the art, M.P.E.P. § 2163(II)(A)(2), the portion of each monomer that is a tetranectin trimerising structural element has been more than adequately described.

With respect to the portion of each monomer that specifically binds a trimeric cytokine, the specification states that the monomers of the disclosed trimeric polypeptides comprise a specific binding member capable of binding a trimeric cytokine (specification, page 6). The specification defines a specific binding member as "a member of a pair of molecules which have binding specificity for one another" (specification, page 8), and defines trimeric cytokines as being "small proteins and fragments thereof, which are produced and secreted by a cell, and which elicit a specific

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response in a cell which has a receptor for that cytokine, e.g. by affecting the growth, division and/or function of the cell" (specification, page 6). The specification also lists a number of examples of trimeric cytokines, including macrophage migration inhibitory factor (MIF) and cytokines within the tumor necrosis factor ligand super family (TNFLSF) (specification, page 7), which includes at least seventeen recognized ligands (*i.e.*, lymphotoxin alpha (LTA), tumor necrosis factor (TNF), lymphotoxin beta (LTB), OX-40L, CD40L, FasL, CD27L, CD30L, 4-1BB-L, TRAIL, RANKL, TWEAK, APRIL, BAFF, LIGHT, VEGI, and GITRL; specification, page 8; *see also* Table 1 on page 7 of specification) that share a conserved trimeric C-terminal domain known as the "TNF homology domain" (THD) (specification, page 7). In addition, the specification lists a number of examples of specific binding members that are capable of binding a trimeric cytokine, including receptors within the tumor necrosis factor superfamily (*e.g.*, TNFRSF1A, TNFRSF1B, LTBR, TNFRSF4, TNFRSF5, TNFRSF6, TNFRSF6B, TNFRSF7, TNFRSF8, TNFRSF9, TNFRSF10A, TNFRSF10B, TNFRSF10C, TNFRSF10D, TNFRSF11A, TNFRSF11 B, TNFRSF12, TNFRSF12L, TNFRSF13B, TNFRSF13C, TNFRSF14, NGFR, TNFRSF17, TNFRSF18, TNFRSF19, TNFRSF19L, TNFRSF21, TNFRSF22, and TNFRSF23; specification, page 10; *see also* Table 2 on pages 9-10. Furthermore, the specification discloses that sequences having the scaffold structure of C-type lectin-like domains (CTLD), such as the human tetranectin-based CTLD, may be capable of binding trimeric cytokines such as TNF (specification, page 12). Applicants contend, therefore, that in view of the disclosure in the specification, one of ordinary skill in the art would readily recognize the types of molecules that are encompassed by the phrase "trimeric cytokine," the types of the molecules that would be capable of specifically binding a trimeric cytokine, and thus, could readily envision the structure of the portion of the claimed trimeric polypeptide that specifically binds a trimeric cytokine.

Applicants respectfully disagree with the Action's assertion that by failing to disclose any monomer other than the monomers of SEQ ID NOs: 106, 107, and 108, Applicants have failed to provide an adequate written description of the claimed trimeric polypeptides. Applicants contend, however, that the disclosure of a representative number of species is but one way to satisfy the written description requirement. The written description requirement may also be satisfied by providing a description of sufficient, relevant, identifying characteristics (*e.g.*, functional characteristics coupled with a known or disclosed correlation between function and structure) for the

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claimed invention. As described above, the specification, when coupled with the knowledge in the art, provides sufficient, relevant, identifying characteristics for both the portion of each monomer that specifically binds a trimeric cytokine and the portion of each monomer that is a tetranectin trimerising structural element.

Applicants also respectfully disagree with the Action's assertion that the facts of either *University of Rochester* or *Noelle* are similar to the situation presented by the instant application. The Action characterizes *University of Rochester* as standing for the proposition that "the inventors could not be said to have 'possessed' the claimed invention without knowing of a compound or method certain to produce the compound." However, the instant application discloses three monomers as well as a description of sufficient, relevant, identifying characteristics for each of the two portions of the monomers that constitute the claimed trimeric polypeptides. In addition, the instant application discloses numerous molecules that specifically bind trimeric cytokines, as well as numerous trimeric cytokines. In contrast, no species falling within the claims were disclosed in *University of Rochester*. Applicants contend that *Noelle* is similarly unhelpful, as the specification discloses numerous molecules that specifically bind trimeric cytokines and numerous trimeric cytokines.

Finally, Applicants also respectfully disagree with the Action's assertion that because more residues in the tetranectin trimerising structural element are non-conserved, the specification fails to provide an adequate written description for the tetranectin trimerising structural element (other than the TTSE of SEQ ID NO: 81). As discussed above, the specification, when coupled with the knowledge in the art (*i.e.*, the express teachings in the '906 publication), establish that the portion of each monomer that is a tetranectin trimerising structural element has been more than adequately described.

In view of the specification's express teachings and knowledge in the art at the time of filing of the instant application (*see, e.g.*, the '906 publication), Applicants contend that the trimeric polypeptides of the instant invention have been described in sufficient detail such that one of ordinary skill in the art would conclude that Applicants had possession of the claimed invention. Applicants therefore contend that claims claims 1, 18-23, 30, and 35 satisfy the written description

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requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this ground of rejection be withdrawn.

b. Rejection of claims 1, 18-23, 30, and 35 under the enablement requirement of 35 U.S.C. § 112, first paragraph

The Office Action also maintains the rejection of claims 1, 18-23, 30, and 35 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. The Action states that the specification, while being enabling for a trimeric polypeptide comprising three monomers, wherein each monomer comprises the amino acid sequence of SEQ ID NOs: 106, 107, or 108, and each monomer further comprises a specific cytokine binding domain and a tetranectin trimerising domain comprising the amino acid sequence of SEQ ID NO: 81, does not reasonably provide enablement for the genus of trimeric polypeptides recited in claims 1, 18, and 19. The Action also states that the rejection is maintained for reasons of record set forth at pages 7-9 of the Office action mailed August 22, 2008.

In addition, the Action states that "the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record," adding that "Applicants arguments that the standard is that of obtaining a subject t[ri]meric polypeptide that has a portion which is a specific binding member capable of binding a trimeric cytokine, and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts." The Action also states that "the instant specification does not provide a description of a repeatable process of producing the claimed trimeric polypeptide whose tetranectin trimerising domain amino acid sequence deviates from the disclosed sequence by as much as 17%," and concludes that "[t]o practice the instant invention in a manner consistent with the breadth of the claims would [require] a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues which are required for functional and structural integrity of those proteins." The Action further states that:

> [I]t is highly improbable that a trimeric protein having a tetranectin trimerising domain with amino acid sequence identity of 87% or 92% identity to that disclosed

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> in SEQ ID NO:81 will more likely than not perform in the manner disclosed and the instant specification does not provide the guidance needed to predictably alter the sequence with any reasonable expectation that the resulting protein will have the desirable activity.

Applicants respectfully disagree with the Action's assertion that the specification is not enabling for trimeric polypeptides other than those comprising the monomers set forth in SEQ ID NOs: 106, 107, or 108. As an initial matter, Applicants respectfully disagree with the Action's assertion that Applicants argued in their previous response that "the standard is that of obtaining a subject t[ri]meric polypeptide that has a portion which is a specific binding member capable of binding a trimeric cytokine, and testing to see if it retains the desired biological activity." Instead, Applicants' prior response focused on the specification's substantial teachings regarding the tetranectin trimerising domain and specific binding members capable of binding a trimeric cytokine. Applicants, however, agree with the Action's statement that a proper examination of compliance with the enablement requirement should be performed using the factors outlined in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." *In re Wright*, 999 F.2d 1557, 1561 (Fed.Cir. 1993); *see also Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991); *In re Fisher*, 427 F.2d 833, 839 (1970). The scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. Whether making and using the invention would have required undue experimentation and thus whether disclosures are enabling is a legal conclusion based upon several underlying factual inquires. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Among the factors to be considered in determining whether any necessary experimentation is "undue" are the nature of the invention, breadth of the claims, state of the prior art, level of skill of those in the art, level of predictability in the art, amount of direction provided by the inventor, existence of working examples, and quantity of experimentation needed to make or use the invention based on the content of the disclosure. *Id.* Thus, to determine whether the specification of the instant application is enabling, a consideration of the *Wands* factors is required.

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a. Nature of the invention

The claimed invention is directed towards trimeric polypeptides comprising three monomers, wherein a first portion of each monomer specifically binds a trimeric cytokine and a second portion of each monomer is a tetranectin trimerising structural element. The specification states that tetranectin trimerising structural elements, which are responsible for trimerisation of the claimed trimeric polypeptides (specification, page 13), are described in detail in International Publication No. WO 98/56906 (the '906 publication; *i.e.*, the PCT equivalent of U.S. Application No. 11/452,434, which is discussed below in section 3). The specification states that the monomers of the disclosed trimeric polypeptides comprise a specific binding member capable of binding a trimeric cytokine (specification, page 6), and defines the terms "specific binding member" and "trimeric cytokine" (specification, pages 6 and 8). The specification also lists a number of examples of trimeric cytokines, including macrophage migration inhibitory factor (MIF) and cytokines within the tumor necrosis factor ligand super family (TNFLSF) (specification, page 7), which includes at least seventeen recognized ligands (*i.e.*, lymphotoxin alpha (LTA), tumor necrosis factor (TNF), lymphotoxin beta (LTB), OX-40L, CD40L, FasL, CD27L, CD30L, 4-1BB-L, TRAIL, RANKL, TWEAK, APRIL, BAFF, LIGHT, VEGI, and GITRL; specification, page 8; *see also* Table 1 on page 7 of specification) that share a conserved trimeric C-terminal domain known as the "TNF homology domain" (THD) (specification, page 7). In addition, the specification lists a number of examples of specific binding members that are capable of binding a trimeric cytokine, including receptors within the tumor necrosis factor superfamily (*e.g.*, TNFRSF1A, TNFRSF1B, LTBR, TNFRSF4, TNFRSF5, TNFRSF6, TNFRSF6B, TNFRSF7, TNFRSF8, TNFRSF9, TNFRSF10A, TNFRSF10B, TNFRSF10C, TNFRSF10D, TNFRSF11A, TNFRSF11 B, TNFRSF12, TNFRSF12L, TNFRSF13B, TNFRSF13C, TNFRSF14, NGFR, TNFRSF17, TNFRSF18, TNFRSF19, TNFRSF19L, TNFRSF21, TNFRSF22, and TNFRSF23; specification, page 10; *see also* Table 2 on pages 9-10. Finally, the specification discloses that sequences having the scaffold structure of C-type lectin-like domains (CTLD), such as the human tetranectin-based CTLD, may be capable of binding trimeric cytokines such as TNF (specification, page 12). Applicants contend that this factor mitigates in favor of enablement.

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b. Breadth of the claims

The claimed invention is directed to trimeric polypeptides comprising three monomers that each comprise a tetranectin trimerising structural element (which is responsible for trimerisation of the monomers) and an amino acid sequence that specifically binds a trimeric cytokine (such as a receptor within the tumor necrosis factor superfamily). The claims do not encompass all trimeric polypeptides, nor do the claims encompass all trimeric polpeptides possessing a tetranectin trimerising structural element. Rather, the claims encompass only those trimeric polypeptides that possess a sequence that specifically binds a trimeric cytokine. Therefore, the claims are not unduly broad. Applicants contend that this factor mitigates in favor of enablement.

c. State of the prior art

The state of the prior art is such that the claimed trimeric polypeptides can be readily prepared. Applicants contend that this factor mitigates in favor of enablement.

d. Level of skill of those in the art

A person with skill in the art could use the teachings provided in the specification and knowledge in the art to readily generate the trimeric polypeptides of the claimed invention. Applicants contend that this factor mitigates in favor of enablement.

e. Level of predictability in the art

It is predictable that the trimeric polypeptides of the claimed invention can be constructed using the teachings of the specification and knowledge in the art. In addition, it is predictable that if each monomer of the claimed trimeric polypeptides contains a tetranectin trimerising structural element, as required by the pending claims, the monomers constituting the trimeric polypeptide will trimerize, thus generating a trimeric polypeptide. Furthermore, it is predictable that if each monomer contains a sequence that specifically binds a trimeric cytokine (such as the sequences disclosed in the specification), the trimeric polypeptide will bind a trimeric cytokine. With respect to the portion of each monomer that is a tetranectin trimerising structural element, Applicants respectfully disagree with the Action's assertion that a "it is highly improbable that a trimeric protein having a tetranectin trimerising domain with amino acid sequence identity of 87% or 92% identity to that disclosed in

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SEQ ID NO:81 will more likely than not perform in the manner disclosed [in the specification (*i.e.*, trimerize)]." Applicants contend, instead, that one of skill in the art could use the teachings of the specification and knowledge in the art to generate a monomer containing a modified tetranectin trimerising domain that would lead to trimerisation of the monomers and yield a trimeric polypeptide. Applicants, therefore, contend that this factor mitigates in favor of enablement.

f. Amount of direction or guidance presented

The specification provides seven examples that teach the preparation of constructs encoding trimeric polypeptides containing TNFRII fragments (Example 2), the preparation of constructs encoding trimeric polypeptides containing TNFRSF13B fragments (Example 6), the preparation of constructs encoding trimeric polypeptides containing TNFRSF Fn14 fragments (Example 7), the preparation of constructs encoding trimeric polypeptides containing TNFRSF13C fragments (Example 8), the preparation of constructs encoding trimeric polypeptides containing CTLD binders for TNF (Example 9), the biological activity (*i.e.*, the inhibition of TNF-alpha-mediated cytotoxicity) of a trimeric polypeptide produced from one of the constructs described in Example 2 (Example 4), and the affinity of trimeric polypeptides containing CTLD binders for TNF (Example 10). When coupled with the other teachings in the specification, and knowledge in the art, Applicants contend that the specification provides adequate direction and guidance to generate the claimed trimeric polypeptides. Applicants contend that this factor mitigates in favor of enablement.

g. Presence/absence of working examples of the invention

The specification provides several working examples for the construction of trimeric polypeptides comprising monomers containing a tetranectin trimerising structural element and a sequence that specifically binds a trimeric cytokine. Among these working examples are Examples 2, 4, 9, and 10. Applicants contend that this factor mitigates in favor of enablement.

h. Quantity of experimentation necessary

The claimed invention is directed towards trimeric polypeptides comprising three monomers, wherein a first portion of each monomer specifically binds a trimeric cytokine and a second portion of each monomer is a tetranectin trimerising structural element. As the specification, when coupled

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with knowledge in the art, teaches tetranectin trimerising structural elements that would allow for treimerisation of the monomers comprising the trimeri polypeptide, only nominal experimentation would be required to generate monomers that would actually form trimeric polypeptides. In addition, as the specification, when coupled with the knowledge in the art, teaches numerous sequences that would specifically bind a trimeric cytokine, some experimentation – but not undue experimentation – would be required to determine whether a trimeric polypeptide binds a trimeric cytokine. Applicants contend that this factor mitigates in favor of enablement.

Applicants contend that the specification is enabling. An examination of the specification in view of the *Wands* factors mitigates in favor of enablement. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Applicants respectfully contend that the rejections based on 35 U.S.C. § 112, first paragraph, have been traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

2. Rejection of claim 21 and 35 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 21 and 35 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action states that claim 21 is vague and indefinite for reciting "SEQ ID NO:106 SEQ ID NO:108" rather than "SEQ ID NO:106, SEQ ID NO:108."

Applicants have amended claim 21 to recite "SEQ ID NO:106, SEQ ID NO:108," and therefore, request withdrawal of this ground of rejection.

The Action also states that claim 35 is vague and indefinite for reciting "mutagenized with to a serine" rather than "substituted with a serine."

Applicants have amended claim 35 to recite "substituted with a serine," and therefore, request withdrawal of this ground of rejection.

3. Provisional rejection of claims 1, 18-20, and 30 for obviousness-type double patenting

The Office Action maintains the provisional rejection of claims 1, 18-20, and 30 under the

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judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56-68 of U.S. Application No. 11/452,434 (the '434 application). The Action states that while the conflicting claims are not identical, they are not patentably distinct from each other for reasons of record set forth at pages 9-11 of the Office action mailed August 22, 2008.

Because the obviousness-type double patenting rejection is provisional, Applicants elect to address this ground of rejection by submitting a Terminal Disclaimer or by argument upon notification that this rejection has been made non-provisional, all other conditions for patentability have been met, and the instant claims are otherwise in condition for allowance.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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Dated: April 13, 2009

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